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EXAMINER	
GROSS, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/944,175	OGURA, NOBUHIKO	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-8 and 10-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Responsive to communications entered 11/12/2007. Claims 1,2,4-8,10-22 are pending. Claims 1,2,4-8,10-22 are examined herein.

In view of the appeal brief filed on 11/12/2007, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

The present application has a filing date of 9/4/2001 and acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to Japanese patent 2000-267449 filed 9/4/2000.

Withdrawn Rejections -35 USC § 102

The rejection of claims 2, 5, 13 and 15 under 35 U.S.C. 102(b) as being anticipated by Ishii et al. (*Nucleic Acids Res.*, **1997**, 25(17), pgs. 3550-3551) is hereby withdrawn upon further consideration.

Maintained Rejections - 35 USC § 112

Claims 1, 2, 4-8, and 10-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of analyzing biochemicals wherein the steps of a) fixing the probes on a substrate, i.e. a "non-covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex of both the probe and capture target are "separated" from the substrate (see instant specification pg. 21-23 and 40-43), does not reasonably provide enablement for the method of analyzing biochemicals wherein the steps of a) fixing the probes on a substrate, i.e. "covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex of both the probe and capture target are "separated" from the substrate. In addition the instant specification does not provide a specific definition for the step of fixing the probes on a substrate such that the broadest reasonable interpretation, i.e. the scope of this step, of this step would include both "non-covalent attachment" of the probe onto the substrate and "covalent attachment" of the probe onto the substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a scope of enablement rejection (see MPEP § 2164.08 and *In re* Goodman, 11 F.3d 1046, 1052, 29 USPQ2d 2010, 2015 (Fed. Cir. 1993)).

Response to Arguments

Covalent Attachment

Applicant argues, see p 12-13 (Appeal Brief entered 11/12/2007) that covalent attachment of probes (i.e. fixing probes selected in advance on a substrate per claim 1) was enabled in the art at the time the invention was made.

The examiner agrees with the contention that it was *possible* to covalently immobilize proteins, albeit unpredictably, at the time the invention was made. Evidence concerning unpredictable nature of receptor immobilization is provided by Muscate et al on p 1422, (1998 Anal Chem 70:1419-1424 – PTO 892 4/10/2006): "Immobilization procedures are often **very time intensive** and have to **specifically developed** for each **receptor**." Emphasis added. Notably, claim 1 is drawn to a specific binding reaction, which includes receptor-ligand reactions, according to paragraph 0062 of the present published application. The examiner submits that protocols concerning covalent immobilization of receptors is unpredictable since time intensive, specific development is necessary for each individual receptor . Likewise, the examiner submits that, in an effort to practice the full scope of the presently claimed subject matter one of skill in the art would need to perform undue experimentation due to unpredictable nature of receptor immobilization chemistry.

Fractionation

Applicant asserts, see p 13-14 (Appeal Brief entered 11/12/2007) that *fractionation* of the combined body of (i) the probe, (ii) the captured target and (iii) a substance derived from a living organism other than the captured target, such as set

forth in claim 1 does not require the combined body of the probe, the captured target and the substance derived from a living organism other than the captured target move *together* as one unit, but rather fractionation may occur merely by separating the probe, target and the substance derived from a living organism other than the captured target *apart* from one another.

It is noted, however, that claim 1 requires element (iii), the substance derived from a living organism other than the captured target be bound with element (i), the probe, due to a similarity in structure. Contrary to the applicant's assertion, the examiner submits that if the substance derived from a living organism other than the captured target is bound with a covalently immobilized probe, it becomes similarly immobilized (i.e. it cannot move).

In other words, giving the claims the broadest reasonable interpretation, "fractionating a combined body of the probe, the captured target and a substance derived from a living organism other than the captured target which is bound with the probe due to a similarity in structure," as set forth in claim 1 reads on both fractionation all three elements **together** as one unit (i.e. as a combined body) as well as fractionating **apart** the target from the combined body.

In response to applicant's argument that the former interpretation fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., separating the target *apart* from the probe and the substance derived from a living organism other than the captured target which is bound with the probe due to a similarity in structure) are not recited in the rejected claim(s). Although

the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Maintained Rejections - 35 USC § 102

Claims 1, 11, 19 and 22 and 4, 10, 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishii et al. (*Nucleic Acids Res.*, **1997**, 25(17), pgs. 3550-3551).

Please note that in this office action, claims 4, 10 and 20 are newly rejected as it was determined, after further consideration, that Ishii et al teach the limitations set forth in said claims 4, 10 and 20 (see below). Also note that this rejection has been completely rewritten to more fully address applicants' arguments.

For the purposes of this rejection, fractionation set forth in claim 1 is taken as one step. For the purposes of this rejection, fixing probes set forth in claim 1 is taken as one step. See 35 USC 112 second paragraph concerns below.

The claimed subject matter per claim 1 is drawn to a biochemical analyzing method comprising the steps of:

[a] fixing probes selected in advance on a substrate;

[b] binding a target with at least one of the probes using a specific binding reaction to capture the target;

[c] fractionating a combined body of the probe, the captured target and a substance derived from a living organism other than the captured target which is bound with the probe due to a similarity in structure;

[d] detecting only a fractionated target; and

[e] quantitatively analyzing the detected target, wherein the probes are spotted on the substrate and fixed thereon, and the combined body of the probe, the captured target and the substance derived from a living organism other than the target is electrophoresed, thereby being fractionated,

wherein during the fractionating, the combined body of the probe and the captured target and the substance derived from a living organism other than the target is separated into a plurality of fractions based on molecular weight.

Claims 11, 19 and 22 and 4, 10, 20 represent variations thereof.

Ishii et al teach, throughout the document and especially the title, abstract and the first full paragraph on p 3550, right column, through the first paragraph on p 3551, a solid-phase assay to screen mouse monoclonal antibodies (mABs), produced by various hybridomas, which is applied toward finding the *Candida albicans* analog of the yeast transcription factor Rap1p. Ishii et al state on p 3551, lines 1-2 that Rap1p in yeast binds ENO1 RPG-box DNA.

In this vein, Ishii et al teach each of said mABs microtiter (probes) were adsorbed in the wells of a microtiter plate containing goat anti-mouse Fc antibodies on p 3550 right column first full paragraph. Said adsorption of said mAB is taken as fixing probes selected in advance on a substrate per claim 1[a] and "the probes are spotted on the substrate and fixed thereon" per claim 1[e]. Ishii et al next bind an antigen (i.e. 70 % purified *Candida albicans* Rap1p analog) thereto. Said *Candida albicans* Rap1p analog is taken the target set forth in claim 1[b].

Each of said wells containing a different mAB were assayed for binding of biotinylated ENO1 RPG-box DNA with avidin labeled horse radish peroxidase based colorimetric assay and the results are tabulated in figure 2a of Ishii et al. A few mMABs, such as 0A4 bound said *Candida albicans* Rap1p analog, having successfully formed the complex illustrated in figure 1a of Ishii et al.

mAB 0A4 (i.e. probe) was combined with ^{32}P labeled ENO1 RPG-box (i.e. substance derived from a living organism other than the captured target which is bound with the probe due to a similarity in structure (i.e. to yeast Rap1p) plus *Candida albicans* extract (i.e. captured target).

Ishii et al performed an electromobility shift assay (EMSA) to better characterize mAB 0A4, as shown in figure 2b lane 2. The band of free ^{32}P labeled ENO1 RPG-box having the smallest molecular weight proceeded the fastest through the gel. The band corresponding to *Candida albicans* Rap1p analog (in *Candida albicans* extract) bound to ^{32}P labeled ENO1 RPG-box was moderately retarded. The band corresponding to the ternary complex of mAB 0A4 bound to the *Candida albicans* Rap1p analog, in turn bound to ^{32}P labeled ENO1 RPG-box had the greatest molecular weight and was super-shifted, proceeding the least through the gel. Said EMSA provides separation (i.e. fractionation) of a combined body of the probe (mAB 0A4), the target (*Candida albicans* Rap1p analog) and a substance derived from a living organism other than the captured target which is bound with the probe (ENO1 RPG-box) as set forth in claim 1[c].

The various electromobilities of said bands meet the limitation "during the fractionating, the combined body of the probe and the captured target and the substance derived from a living organism other than the target is separated into a plurality of fractions based on molecular weight" as set forth in the second wherein clause of claim 1.

Said EMSA of Ishii et al represents a type of electrophoresis, meeting the limitation " the combined body of the probe, the captured target and the substance

derived from a living organism other than the target is electrophoresed, thereby being fractionated" set forth in claim 1[e].

As *only* the ternary complex was super-shifted toward the top of the lane 2, the EMSA of Ishii et al affords detecting *only* a fractioned target, as set forth in claim 1[d]. See also 35 USC 112 second paragraph considerations below concerning "detecting *only* a fractionated target."

Ishii et al teach in the legend to figure 1, said EMSA radioactivity was quantitatied, therein providing the quantitatively analyzing step 1 [e] of claim 1.

Said microtiter plate of Ishii et al was read in the manner of Kemp et al (1989 PNAS 86:2423-2427); See Ishii et al reference 5. Evidence provided in figure 4 of Kemp et al show a microtiter plate as consisting of a series wells in rows, therein reading on the 1 dimensional spotting regimen set forth in claim 10.

Said series of rows in said microtiter plate together provide a two dimensional grid, again illustrated in figure 4 of Kemp et al, therein providing the two dimensional spotting set forth in claim 11.

Further shown in figure 4 of Kemp et al, said grid is colormetrically analyzed, which is taken as providing the two dimensional scann[ing] and light released from the targets is detected with an area sensor, as set forth in claims 19-20.

The examiner submits that electrophoresis being performed at an angle with the surface of the substrate, as set forth in claim 4 is inherently taught by Ishii et al, as there are no limitation regarding the degree of said angle in claim 4.

Response to Arguments

Applicant argues, see p 14 third full paragraph (Appeal brief entered 11/12/2007) that Ishii et al do not disclose steps c-e and the wherein clause set forth in claim 1. In particular, applicant argues, see p 15 third full paragraph (Appeal brief entered 11/12/2007). Ishii et al do not teach "fractioning a combined body", "detecting only a fractionated target", "quantitatively analyzing the detected target".

The examiner submits that those limitations and the wherein clause(s) are now more fully addressed in the newly written rejection above.

Applicant asserts, see paragraph bridging pp 14-15 through p 15 first paragraph, (Appeal Brief entered 11/12/2007) that *fractionation* of the combined body of (i) the probe, (ii) the captured target and (iii) a substance derived from a living organism other than the captured target, such as set forth in claim 1 does not require the combined body of the probe, the captured target and the substance derived from a living organism other than the captured target need not be fractioned *together* as one unit, but rather the plain meaning of fractionation means subjecting the combined body to fractionation.

Furthermore, applicant asserts, see p 15 second full paragraph (Appeal Brief entered 11/12/2007) that lane 2 of figure 2b of Ishii does not subject the combined body the probe, the captured target and a substance derived from a living organism other than the captured target to fractionation because mAB 04A would immunoprecipitate the DNA binding complex, according to Ishii et al which is reflected in the super-shifted complex. Applicant contends that the super-shifted complex represents "unfractionated 'fractionation.'"

In this regard it is noted, applicant admits in the sentence bridging p 13-14 of the appeal brief (11/12/2007) "A probe can be fractionated from a combined body by **remaining stationary** while the target and the substance other than the target move." Emphasis added. Here, mAB 0A4 (i.e. probe) *remains stationary* (i.e. super-shifted) while the *Candida albicans* Rap1p (i.e. target) and ENO1 RPG-box (i.e. substance other than the target) move. The examiner respectfully submits that the EMSA assay of Ishii et al provides the type of fractionation described by applicant on p 13-14 of the appeal brief, with mAB 0A4 remaining stationary, in contrast with applicant's assertion, that the super-shifted complex is unfractionated. Thus, the EMSA assay of Ishii et al reads on the fractionating step 1[c] of claim 1.

New Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1,2,4,12,13,15,22 are rejected under 35 U.S.C. 102(e) as being anticipated by **Gerdes et al** (US Patent 6,291,166).

For the purposes of this rejection, fractionation set forth in claim 1 is taken as one step. For the purposes of this rejection, fixing probes set forth in claim 1 is taken as one step. See 35 USC 112 second paragraph concerns below.

Gerdes et al teach, throughout the document and especially claim 1 and column 11 and the paragraph bridging columns 10 and 11, a method of archiving nucleic acids by irreversibly binding to a electropositive solid phase matrix which can be used to detect, for instance, genes of infectious agents.

In particular, Gerdes et al teach in examples 8-10, solid-phase rtPCR amplification of HIV RNA immobilized on aluminum oxide particles. Said immobilized HIV RNA is taken as providing the fixing probes step set forth in claim 1. In the process of said amplification, discussed in detail in examples 1 and 4, primers, reverse transcriptase and Taq DNA polymerase are typically added in an effort to generate an amplification product, which binds to said HIV RNA by hybridization. An amplification product is taken as providing the 'binding a target' step of claim 1. Gerdes et al teach in figure 11, agarose gel electrophoresis in effort to fractionate the immobilized HIV RNA probe and primers from the amplification product target, which is taken as providing the fractioning by electrophoresis with separation a plurality of fractions based on molecular weight of claim 1. See molecular weight ladder lane on the left of figure 11. The third lane shows detection of only the pcr amplification product target, as set forth in claim 1[d]. See also 35 USC 112 second paragraph considerations below concerning "detecting *only* a fractionated target." Said primers are taken as a substance derived from a living organism other than the captured target which is bound to the probe due to a similarity in structure.

Said amplification product is bound to the HIV RNA using hybridization, such as set forth in claim 2.

The examiner submits that electrophoresis being performed at an angle with the surface of the substrate, as set forth in claim 4 is inherently taught by Gerdes et al, as there is no limitation regarding the degree of said angle in claim 4..

Said genes of infectious agents are taken as the target gene of claim 12.

Gerdes et al teach ethidium bromide staining, in for example figure 5, which is taken as meeting the limitations concerning a fluorescent substance set forth in claims 13 and 15.

New Claim Rejection(s) – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,2,4,12,13,15,22 and 5,6,7,8,14,21 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Gerdes et al** (US Patent 6,291,166) in view of **Briggs et al** (US Patent 5,560,811 – PTO-1449 entry 5/3/2004).

For the purposes of this rejection, fractionation set forth in claim 1 is taken as one step. For the purposes of this rejection, fixing probes set forth in claim 1 is taken as one step. See 35 USC 112 second paragraph concerns below.

Gerdes et al is relied on as above.

Additionally, Gerdes et al teach an embodiment in claims 3 and 4 that said electropositive solid phase matrix may be in the form of a planar blot or microarray.

Gerdes et al do not teach: a block of gel adjacent and in contact with a substrate (claims 5 and 6); a plurality of gel filled capillaries (claims 7 and 8); labeling a target with a fluorescent substance prior to the target binding with the probes (claim 14); three dimensional scanning (claim 21).

Briggs et al teach, throughout the document and especially figure 4 and column 3, lines 57-64, a capillary electrophoresis system, comprised of a three dimensional block of plural capillaries stacked above an array of samples, reading on claim 6.

Briggs et al teach in example 1, said capillaries may filled with fused silica derivatized with 3.5 % linear polyacrylamide (a gel), as set forth in claims 7 and 8.

Briggs et al teach in example 2, separation of a series of single-stranded oligonucleotides, each labeled with the fluorophore FAM, which is taken as labeling a target with a fluorescent substance prior to binding with the probes, as set forth in claim 14.

The examiner submits that the sum of quantitative data obtained in each of said capillaries, such shown in figure 19, of Briggs et al generates a quantitative three dimensional scan with respect to capillary no. vs. time vs. fluorescence, thereby providing a three dimensional scan concerning light released from targets, such as set forth in claim 21.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to utilize the three dimensional capillary electrophoresis block of Briggs et al with the electropositive microarray per Gerdes et al. In particular, the arrangement shown in figure 4 of Briggs et al used in concert with the

electropositive microarray per Gerdes et al meets the limitations set forth in claim 5, with the sipper capillary, element 82 of Briggs et al, adjacent and in contact with the electropositive microarray of Gerdes et al.

One of ordinary skill in the art would have been motivated to use the three dimensional capillary electrophoresis block of Briggs et al with the electropositive microarray per Gerdes et al because capillary electrophoresis requires only 1-5% the amount of sample as a standard gel, thus reducing reagent cost or amplification time as noted by Briggs et al in 6, lines 7-10, thereby providing less expensive assays in less time.

One of ordinary skill in the art would have had a reasonable expectation of success in combining the three dimensional capillary electrophoresis system of Briggs with the electropositive microarray per Gerdes et al because both Briggs et al and Gerdes et al are concerned with nucleic acid detection by PCR amplification and gel electrophoresis, as reflected in figure 14 of Briggs et al and figure 5 of Gerdes. Therefore, the method of Gerdes et al, lies well within the scope of the capillary electrophoresis system of Briggs.

Claims 1,2,4,12,13,15,22 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Gerdes et al** (US Patent 6,291,166) in view of **Akhavan-Tafti** (US Patent 6,126,870).

For the purposes of this rejection, fractionation set forth in claim 1 is taken as one step. For the purposes of this rejection, fixing probes set forth in claim 1 is taken as one step. See 35 USC 112 second paragraph concerns below.

Gerdes et al is relied on as above.

Gerdes et al do not teach: a chemiluminescent labeling substrate (claim 16) used prior to the binding step (claim 17) or after fractionation (claim 18).

Akhavan-Tafti teaches, throughout the document and especially claim 1, the abstract and column 1, lines 20-22, small efficient chemiluminescent labeling compounds based on acridan, applied toward, for example, detecting nucleic acids and proteins, particularly in an electrophoresis gel.

Akhavan-Tafti teaches in figure 3B and column 40, chemiluminescence based detection of BSA labeled with $APCN_2$ (i.e. acridan derivative 26), to generate BSA-$APCN_2$. Said pre-labeled BSA-$APCN_2$ protocol set forth in column 40 of Akhavan-Tafti affords chemiluminescent substrate labeling before target binding, as set forth in claims 16 and 17.

Akhavan-Tafti teaches said acridan derivatives may also be used for Northern and Southern blotting in column 16, line 47. Said Northern or Southern blots are performed after an electrophoretic fractionation, thus providing the limitations set forth in claim 18.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to utilize the small efficient chemiluminescent

labeling compounds based on acridan per Akhavan-Tafti for gene detection of an archived target species (amplification product) of Gerdes et al.

One of ordinary skill in the art would have been motivated to use the small efficient chemiluminescent labeling compounds based on acridan per Akhavan-Tafti for gene detection of an archived target species (amplification product) of Gerdes et al because acridan derivatives are stable on extended storage and not subject to side reactions, as noted by Akhavan-Tafti in column 2, lines 19-20 which is important for long term archiving.

One of ordinary skill in the art would have had a reasonable expectation of success in applying the small efficient chemiluminescent labeling compounds based on acridan per Akhavan-Tafti toward gene detection of an archived target species (amplification product) of Gerdes et al because both Akhavan-Tafti and Gerdes et al detect nucleic acids by gel electrophoresis. Therefore the acridan chemiluminescent compounds of Akhavan-Tafti lies well within the scope of nucleic acid archiving according to Gerdes et al.

New Claim Rejections - 35 USC § 112

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,2,4-8,10-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Please note the following line numbers are with respect to the Claims Appendix entered 12/20/2007, part of the Appeal Brief entered 11/12/2007.

The phase "in advance" in claim 1 is a relative term which renders the claim indefinite. The phrase "in advance" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, it is not clear if the probes should be fixed in advance of the following steps of claim 1 or perhaps in advance of the 2008 Summer Olympics.

Claims 1,4,5,6,7,15 each recite the limitation "the probe" (singular). There is insufficient antecedent basis for this limitation in the claim. Notably, probes (plural) appears in line 1 of claim 1.

Claim 1 recites the limitation "the detected target" in line 8. There is insufficient antecedent basis for this limitation in the claim. It would appear, this should read the detected fractionated target.

Claim 1 recites vague and indefinite language in “wherein the probes are spotted on the substrate and fixed thereon” in lines 8-9. It is not clear if this constitutes a second fixing step, or if it limits the fixing step in claim 1 line 1. The ambiguity regarding numbers of fixing steps also makes the recitation of the spots being fixed thereon in dependent claims 10 and 11 ambiguous

Claim 1 recites vague and indefinite language in “the combined body of the probe, the captured target and the substance derived from a living organism other than the target is electrophoresed, thereby being fractionated” in lines 11-13. It is not clear if

this constitutes a second fractionation step (i.e. present tense being fractionated) employing electrophoresis, or if it limits the fractionation step (i.e. past tense having been fractionated) in line 4 of claim 1. Along the same line, it is not clear if the clause "wherein the fractionating, the combined body of the probe, the captured target and the substance derived from a living organism other than the target is separated into a plurality of fractions based on molecular weight" in lines 12-14 of claim 1 refers to one or both of said fractionation step(s). The ambiguity regarding numbers of fractionation and/or electrophoresis steps also makes the recitation of fractionation in dependent claims 4,5,6,7,15,18,19,20-22 ambiguous.

Claim 1 recites vague and indefinite language in "detecting *only* a fractionated target" in line 8. Detecting *only* may be interpreted to mean a manner of detection which only is sensitive to a fractionated target species, or else detection of many fractionated species with discernment of the target. It is suggested applicant delete the offending term "only."

Claim 22 recites vague and indefinite language in "wherein targets electrophoresed to positions in accordance with the kinds of the targets are quantified and analyzed" in lines 1-3. It appears there is a missing word and/or grammatical incongruity.

In accordance with MPEP 2173.02: If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C.

112, second paragraph, would be appropriate. See Morton Int 'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

As currently written, the metes and bounds of claim 1, at least, are unascertainable for the reasons raised above. Therefore, claim 1 and all dependent claims are rejected under 35 USC 112, second paragraph.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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